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WEAK, BUT COMPLEX PULSED MAGNETIC FIELDS MAY REDUCE DEPRESSION FOLLOWING TRAUMATIC BRAIN INJURY[1]

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Summary.—Many patients who display psychological depression following a traumatic brain injury do not respond completely to antidepressant drugs. We hypothesized that this type of depression is strongly correlated with subclinical, complex partial seizure-activity within the hippocampal-amygdaloid region that continues for months to years after apparent neurological and behavioral "recovery." Four depressed patients who had sustained traumatic brain injuries and who exhibited mild to moderate brain impairment according to standardized tests received 30 min. of weak (1 μT) burst-firing magnetic fields across the temporal lobes once per week for 5 weeks. There was a significant improvement of depression and reduction of phobias while physical symptoms and other complaints were not changed.

Symptoms attributed to psychological depression are common sequelae to traumatic brain injury (Persinger, 1993b, 1994). Although one traditional response by medical practitioners is to prescribe antidepressant medication, the rationale and the anticipation of successful treatment are derived from clinical trials that involved patients who were depressed in response to psychosocial factors rather than to trauma-induced etiologies. The symptoms of postconcussional and posttraumatic depression may result from neuroelectrical and neurochemical anomalies that differ from the synaptic changes associated with the more typical age-related, sociopsychologically induced depressions.

During the last ten years, the Laurentian Neuroscience Group (e.g., Persinger & Makarec, 1993) as well as R. J. Roberts and associates (Roberts, Gorman, Lee, Hines, Richardson, Riggle, & Varney, 1992) have pursued the hypothesis that a spectrum of complex partial epileptic-like symptoms are frequent consequences of mild to moderate brain trauma. The rationale is derived from the general premise that inhibitory interneurons are extremely vulnerable to the consequences of mechanical energy propagated through the skull into brain space. Typical consequences would include increases in (1) the release of corticotrophin releasing factor, (2) anomalous activity within the hippocampal-amygdaloid complex, and (3) the numbers of disruptions within the neuroelectrical processes that maintain reciprocal inhibition

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between hemispheres. These periods of anomalous, interhemispheric intercalations would be associated subjectively with "sudden depression or panic," an aversive "sense of a presence," or experiences that do not appear to originate from "the self" (Persinger, 1994).

Extreme and protracted paroxysmal but subclinical activity within the hippocampal-amygdaloid formation would be associated with a complete failure of long-term consolidation of memory. The consequences would be exhibited as an interval of posttraumatic amnesia (PTA) for the period following the brain trauma. Intermittent, briefer episodes following resolution of the clinically obvious posttraumatic dysmnesia would contribute to patients' experiences of "memory blanks" and to the reports by the spouses of the patients' anterograde dysmnesia. These dysmnesic episodes may persist for years after the brain trauma and would be exacerbated following behavioral events that release the cascade of corticotrophin releasing factor (an epileptogenic peptide), corticotrophin (from the pituitary), and cortisol.

About one-third of patients with diagnosed complex partial epilepsy also exhibit depression, although the etiology is attributed to other stimuli (Robertson, Trimble, & Townsend, 1987). Recent metabolic measures have shown that many depressed patients exhibit a significant increase in metabolic activity within the amygdaloid-hippocampal region and a decrease in activity within the temporal and (left) prefrontal cortices and traditional antiepileptic compounds such as carbamazepine (Tegretol) and valproic acid (Depakene) have been employed to treat refractory depression (Joffe & Calabrese, 1994). These observations are consistent with the hypothesis that a significant portion of patients who display depression and complex partial epilepsy (with a limbic focus) share similar neuroelectrical or neurochemical processes. Our working model is that the majority of patients who report and display persistent symptoms of depression following a closed head injury and correlative mild to moderate brain impairment also exhibit this type of limbic lability.

Application of magnetic fields that penetrate into the brain has been suggested as a possible method by which the neurons mediating depressive syndromes could be addressed (Zyss, 1994). Researchers reasoning from the principles of classical physics contend that relatively strong (1 Tesla) field strengths are required. For example, George, Wasserman, Williams, Callahan, Ketter, Basser, Hallet, and Post (1995) assumed that, if the left prefrontal cortex is dysfunctional in depression, then repetitive transcranial magnetic stimulation over this area should activate those neurons and improve the symptoms. These authors found that administration of magnetic fields to the left prefrontal cortex each morning for at least five days to six medication-resistant patients with primary mood disorders, significantly decreased symptoms of depression. The mean and standard deviations for the Hamil-

ton Depression scale were 23.8 and 4.2 before the treatment and 17.5 and 8.4 after the treatment (estimated η^2 would be about 70%); however, only two (of the six) patients exhibited clinical improvement.

Other researchers (Jacobson, 1994; Persinger, Richards, & Koren, 1994; Richards, Persinger, & Koren, 1996; Sandyk, 1994a, 1994b, 1995) contended that the *information* content of the applied signal is more critical than the magnitude. From this perspective the functional neural networks mediating neurocognitive processes are more optimally described by models of neuroelectromagnetic resonance or "narrow-band" processes within neural patterns or nets that respond to information (John, 1990). Although the conflict between methodologies that emphasize "meaning" of the stimulus versus the "magnitude" of the stimulus is frequent in science, the positive contributions of one technology to effective treatment do not necessarily imply the negation of the other.

Disruption of the microneuroelectrical processes that slowly escalate into sustained subclinical, complex partial conditions may require minimal energies if the parameters of the applied field employ disruptive properties and they are initiated before the numbers of recruited neurons achieve a critical mass. Recently Bureau and Persinger (1995) reported that the threshold for overt limbic seizures was elevated if the rats were exposed for approximately 1 ksec. to a 50 μT (microTesla) pulsed field once every two to three days. When human beings are exposed to similar pulsed, complex fields but at lower intensities (1 μT), they report most of the experiences (Persinger, 1993a; Ruttan, Persinger, & Koren, 1990) associated with neurosurgical stimulation (Bancaud, Brunet-Bourgin, Chauvel, & Halgren, 1994). Four weekly, 30-min. exposures to these field parameters did not produce adverse effects in normal volunteers (Gillis & Persinger, 1993).

The purpose of the present study was to test the feasibility of externally applying weak, complex magnetic fields through the brain to help reduce psychological depression in patients who still exhibit mild to moderate brain impairment after a neurologically verified, acquired brain injury. We reasoned that, like aspirin which does not influence core body temperature if a person is euthermic but clearly elicits an antipyretic effect if the person displays a fever, the neuroprocesses of this type of postconcussional depression would be particularly sensitive to weak, complex applied magnetic fields. If the effects of these weak, complex electromagnetic fields were considered to have any potential clinical utility, it should be evident with only four subjects who are exposed once per week for only five weeks. If a significant effect was not obvious during this period, then the feasibility of ultimately supplementing or replacing pharmacological treatments with this technology would be minimal.

Two male (ages 34 and 37 years) and two female (ages 40 and 45 years)

patients who had completed neuropsychological assessments were referred to the first author. All of these patients had sustained a closed head injury (2 within 12 months, 1 within 3 years, and 1 about 6 years before treatment began) and displayed mild to moderate brain impairment as defined by the Halstead-Reitan Index, toe graphaesthesia (Persinger & Richards, 1995), and a standardized aggregate of 31 subtests (Persinger, 1995). They also showed impaired dichotic word-listening performance and abnormally elevated scores for a scale from which one may infer complex partial epileptic-like signs (Roberts, *et al.*, 1992). All four patients had reported persistent or frequently intermittent (often with sudden onset) depression, as diagnosed by their physicians, that had not responded to any traditional antidepressant medications.

Because the limits of all conventional medical and psychological interventions had been approached, the patients were considered eligible as candidates for the experimental treatment. Each patient volunteered for the treatment after the potential risks and benefits had been described fully. The consent form indicated that there was some evidence that (1) the application of these fields has been associated with pleasantness (Persinger, *et al.*, 1994; Richards, *et al.*, 1993), (2) there was no clear scientific evidence that brief exposures to these fields had any long-term adverse effects, (3) they could withdraw from the experiment at any time, (4) they could call the second experimenter at any time if questions or symptoms emerged, and (5) the treatment would be given without cost to the patient.

Once per week for five successive weeks each patient met the experimenter within the same room. After a brief social exchange, the patient completed the Beck Depression Inventory (Beck & Steer, 1987), the Symptom Check List-90 (Derogatis, 1994), and the Wahler Physical Symptoms Checklist (Wahler, 1973). The rationale for completion of the inventories at the beginning of each session was to ascertain the persistence of any effect between treatments rather than after treatments. The patient then sat in a comfortable chair within an acoustic chamber. As described elsewhere (Richards, *et al.*, 1993), a complex, burst-firing magnetic field (1 microT) was applied along and through the temporoparietal regions through pairs of four solenoids embedded in small, 10-cm by 7-cm containers attached over the scalp by adhesive strips. The field was delivered once every 4 sec. by a computer. At the end of the 30-min. session, the experimenter discussed any concerns the patient may have had during the previous week and restructured or offered suggestions for any emerging problems. The entire interaction required about one hour.

Although placebo or sham-field conditions would be optimal from an experimental perspective, the concern for the patients (as indicated by their standardized scores on the measures of depression and anxiety) dictated that

all patients receive the treatment and be (indirectly) monitored by both experimenters. We assumed that the problem of placebo effects could be partially accommodated by requiring an extremely large effect size that would be evident with only four patients. An effect size of at least 50% (equivalent to an $r > .70$) of the variance in change of symptoms over a 5-wk. period should exceed the size of an effect from placebos, particularly if the change in scores were stable. Although some researchers would prefer random allocation to sham-field conditions, we concluded that treating all of the subjects and then assessing the strength of the treatment upon scores for depression would satisfy both experimental and humanist considerations.

All analyses involved SPSS on a VAX 4000 computer. A two-way analysis of variance with one level repeated (the five sessions) and one not repeated (sex) were completed for the mean total scores on the Beck Depression Inventory, the Physical Symptoms scores, and for scores on each of the nine scales (compulsion, phobia, hostility, depression, anxiety, paranoia, interpersonal sensitivity, psychasthenia, and psychoticism) from the Symptom Check List-90. There were no significant differences between sexes ($F_{1,2} < 1.00$, $p > .05$) or interactions between sex and sessions.

There were only two significant changes over time (all dfs = 4,8). There was a significant decrease in Beck Depression scores ($F = 4.22$, $p < .04$; partial $\eta^2 = 67\%$) over the five weeks. The means and standard deviations for the Beck Depression scores were 33 ($SD = 9$), 27 ($SD = 7$), 20 ($SD = 10$), 21 ($SD = 8$), and 17 ($SD = 9$), respectively. *Post hoc* paired t tests indicated that the effect was due to the attenuated depression between the first two sessions and the last three sessions. There was also a decrease in the magnitude of phobias ($F = 6.43$, $p < .01$; $\eta^2 = 76\%$). The means and standard deviations were 72 ($SD = 11$), 66 ($SD = 12$), 64 ($SD = 15$), 59 ($SD = 17$), and 56 ($SD = 16$) over the five weeks. There were neither main effects for gender nor interactions between gender and the within-subject measures for these variables. None of the other measures exhibited a significant decrease over time.

The results of this study indicate that four successively assigned patients who displayed persistent depression and complex partial epileptic-like indicators after a closed head injury (mild to moderate brain impairment) and who were refractory to (antidepressant) medication responded positively to a procedure that involved the brief 30-min., weekly application of burst-firing magnetic fields over the temporal lobes. The specificity of the effect is suggested by the change primarily for scores on the Beck Depression Inventory and the scale from which one may infer phobias (frequent symptoms, particularly after motor vehicle incidents). Although the mean scores for the depression scale of the Symptom Check List-90 did not achieve statistical significance, the attenuation of these scores over time approached this criterion

($F = 3.01$, $.10 > p > .05$; $\eta^2 = 60\%$) and also showed a mean decrease of 1.5 standard deviations (change in T score of 15 standardized units).

There are several limitations to this study. In addition to the absence of sham-field controls, we did not assess the continuity of the effect one week and ten weeks after the treatment had been completed. The role of the experimenter and the effects of the posttreatment discussion concerning personal issues during the previous week cannot be quantitatively removed from the effect. [One patient sent an unsolicited letter which stated an appreciation for the treatment, a reduction of the depression and thanks to the first author.] However, both quantitative (unpublished data, $n = 11$ patients) and qualitative evaluations of this population of patients have indicated that this magnitude of improvement does not normally occur within five weeks, even with casual contact about once per week from health professionals. An ABAB design, although experimentally elegant, was not considered ethically appropriate because (1) repeated stimulations were considered to be critical to the elicitation of the effect and (2) variability in the continuity of the attenuation of the depressive, aversive symptoms was considered counterproductive to the maintenance of the more adaptive behaviors emerging during the treatment.

Despite these limitations, the employment of weak, complex fields which may interfere with the limbic electrical activity that generates depression could be a supplementary procedure to traditional techniques. Electroconvulsive shock (ECS) has been considered an effective treatment for severe depressions that are refractory to pharmacological intervention. With this technique, current densities from highly redundant (symmetrical) wave forms are applied to one or both temporal lobes to induce paroxysmal discharges. The neuromechanism for the antidepressive consequences of massive surges of current across the temporal lobes (similar intensities of current applied across the brain stem would be fatal) is not clear (George, *et al.*, 1995). If the functional consequence of this massive current induction is to inhibit the disinhibited limbic structures, then the efficacy of this process for some patients who exhibit depression could be rationalized.

We suspect that the large electric currents associated with electroconvulsive shock are effective indirectly because they may damage the nonmyelinated varicosities of fibers from the locus ceruleus (noradrenaline), the ventral tegmentum, including the substantia nigra compacta (dopamine), and the median raphe (serotonin). When the cell bodies of these aggregates respond (to the insult) by reactive synaptogenesis and reconstruction of their processes, there is an epiphenomenal increase in the synthesis of neurotransmitters, unocclusion of the receptors inactivated by the depression process, and reactive protrusions of the axonal varicosities. Such changes would attenuate the interference with postsynaptic sequestering of these transmitters

whose behavioral manifestation had been psychological depression. The mood would improve.

There may be other less invasive technologies that can be as effective as electroconvulsive shock without its side effects or risks. There is now converging theoretical (Jacobson, 1994) and empirical evidence (Richards, *et al.*, 1993, 1996) that very weak, applied complex magnetic fields whose wave structure and pulse patterns are congruent with groups of neurons within specific regions of brain volume can improve neurocognitive function (e.g., Sandyk, 1994a, 1994b, 1995) in human beings. There may also be effects that facilitate the therapeutic process. For example, one consequence of application of complex fields to the right hemisphere of normal volunteers is the enhancement of poststimulation suggestibility (Tiller & Persinger, 1994). The magnitude of this effect would be sufficient potentially to augment the effects of brief, posttreatment cognitive restructuring upon patients' subsequent behaviors by increasing the reward value of the more adaptable attributions, perceptions, and solutions to personal problems.

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